The Cost-Effectiveness of Immunotherapies for Advanced Biliary Tract Carcinoma: A PRISMA Systematic Literature Review

EPA

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SUMMARY

OBJECTIVES

- Chemotherapy options for unresectable, locally advanced or metastatic biliary tract cancer (BTC) are limited with poor therapeutic outcomes.
- This study aimed to review published literature on the economic impact of immunotherapies for BTC and to identify key drivers that impact cost-effectiveness.

METHODS

- A comprehensive systematic literature review involving electronic databases and grey literature was conducted.
- Studies that assessed the cost-effectiveness of immunotherapies for advanced BTC and were published before January 2025, were included.
- Cochrane collaboration methods and PRISMA guidelines for SLRs were followed.

FINDINGS

- 7 CEAs investigating the use of pembrolizumab and durvalumab were retrieved (**Figure 1**).
- Immunotherapy options for BTC are limited, and that their cost-effectiveness when compared to SoC is dependent on the cost of treatment, utility discount rate, and utility of PD and PFS.
- To our knowledge, **this is the 1st published SLR of CEAs for BTC.**

BACKGROUND & AIMS

- Biliary tract cancer (BTC), including cholangiocarcinoma and gallbladder cancer is the second most common primary hepatic malignancy and accounts for <1% of all human cancers.[1]
- Although rare, BTCs are often identified at an advanced stage and have poor prognoses. Presently, surgery is the only curative option for BTC and the cisplatin–gemcitabine doublet chemotherapy is the current standard of care (SoC) first-line treatment for advanced BTC, with limited treatment outcomes.[2]
- This review aimed to systematically identify the cost-effectiveness analyses (CEAs) of immunotherapies which have emerged in recent years as efficacious additives to current SoC in advanced BTC.

METHODS

- A PRISMA-adherent systematic literature review was undertaken to identify relevant cost-effectiveness analyses (CEAs) and cost-utility analyses published in the English language before 1st February 2025.[3]
- Electronic database searches were conducted in Embase, MEDLINE(R) ALL, and the Cochrane Library via Ovid with supplementary searches undertaken in key cholangiocarcinoma congresses, Google Scholar, the Cost-Effectiveness Analysis register, the International Health Technology Assessment (HTA) database and the NIHR HTA database.
- The peer-reviewed search strategies used a combination of sophisticated subject headings, text words, synonyms and Boolean combination techniques.
- Two reviewers independently screened the literature, extracted data from full publications, and assessed methodological quality using the Drummond 10-item rated checklist.[4]
- The eligibility criteria for screening in the review are shown in **Table 1**.

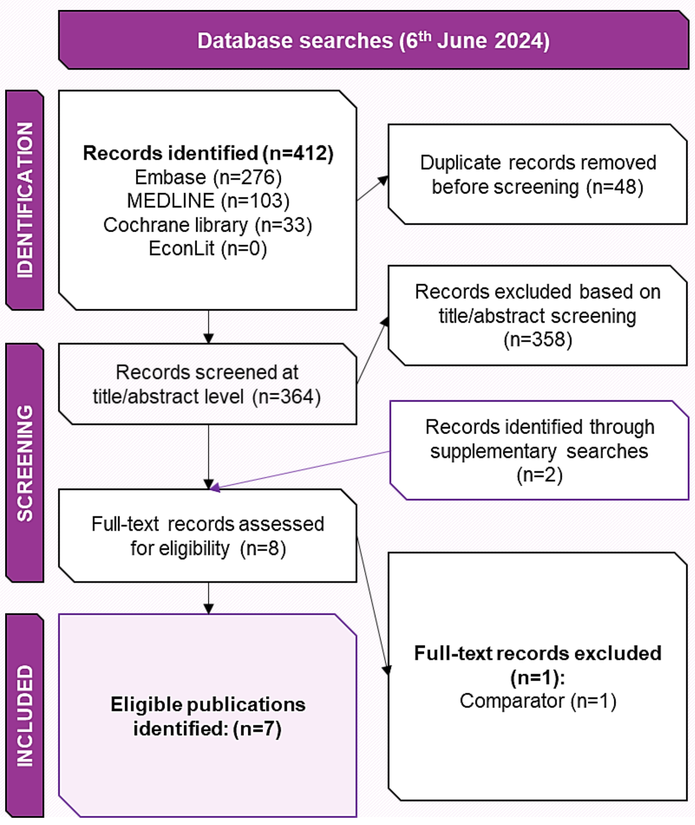
Table 1. Inclusion/exclusion criteria.

Criteria	Inclusion	Exclusion
Population	Adults with advanced (unresectable or metastatic) biliary tract carcinoma (BTC)	Individuals aged <18 years Individuals with a condition other than advanced BTC
Intervention	Any immunotherapy alone or in combination	Interventions not recommended, marketed or used for the treatment of advanced BTC
Comparator	Any chemotherapy alone or in combination	Surgery Radiotherapy Hormonal therapy Alternative medicines
Outcomes	Study design or model structure Treatment costs and health outcomes Cost effectiveness estimates Cost drivers and modelling assumptions	Studies not reporting any outcomes of interest
Study design	Economic evaluations including cost-effectiveness and cost-utility analyses	Non-economic assessments
Limitation(s)	English language publications	Non-English language publication with non-English abstract

RESULTS

- Of the 366 individual articles identified, 7 CEAs met the eligibility criteria. Overall, the reporting quality was assessed as high with 71% of these studies scoring ≥8 points on the Drummond 10-item checklist.
- The cost-effectiveness of immunotherapy in BTC was investigated using China (n=6), United States (US) (n=3), and UK (n=1) healthcare payer perspectives.

Figure 1. PRISMA flow diagram.



- **Immunotherapies investigated:** Analyses considered pembrolizumab (n=4) or durvalumab (n=4) in combination with gemcitabine and cisplatin doublet chemotherapy, at first-line therapy.
- **Model structures**: Analyses favoured using a Markov model or partitioned survival model with three mutually exclusive health states (progression-free survival [PFS], progressed disease [PD], and death).
- **Sources of model inputs**: Efficacy and safety data were derived from the KEYNOTE-966 (NCT04003636) or TOPAZ-1 (NCT03875235) trials. Cost and utility data were obtained from national price registers and/or published literature.
- **Cost-effectiveness threshold**: CEAs used willingness-to-pay (WTP) thresholds of $100,000 and $150,000 per quality-adjusted life year (QALY) or followed the World Health Organization's recommendations to use 3x the country's per capita GDP.
- **Cost of immunotherapy:** The cost of durvalumab plus chemotherapy ranged from $97,629 on a charity assistance plan to $204,123 in China, and $217,069 in the US. While the cost of pembrolizumab plus chemotherapy in China ranged from $88,745 to $113,359, and $210,344 in the US.
- **Incremental cost-effectiveness ratio (ICER):** The ICERs for pembrolizumab compared to systemic SoC ranged from $354,679 to $564,895 in China and $761,371 to $1,109,463 in the US, while durvalumab's ICER ranged from $159,645 with charity assistance to $367,609 in China and $206,223 to $381,864 in the US.
- **Neither immunotherapy option was considered cost-effective** (0% probability) compared to cisplatin–gemcitabine SoC at WTP thresholds.

CONCLUSIONS

- We identified 7 CEAs which assessed durvalumab or pembrolizumab compared to cisplatin–gemcitabine doublet chemotherapy.
- Across studies, model robustness was analysed through one-way sensitivity analyses and probabilistic sensitivity analyses.
- For Chinese and American BTC patients undergoing first-line treatment, neither durvalumab nor pembrolizumab offers a cost-effective advantage to recommended chemotherapy.
- **Key drivers of cost-effectiveness** included the **cost of immunotherapy**, the utility of PD and PFS, the discount rate applied to outcomes, and the proportion of patients receiving subsequent treatment.
- Further analysis of the price of immunotherapy demonstrated that immunotherapy + chemotherapy is only cost-effective at price reductions of 67.4% to 80.9%. Therefore, at current WTP thresholds in China and the US, drug price reductions are necessary.
- Although anti-PD-1/ PD-L1 antibodies improve survival in advanced BTC, they are not cost-effective options at current drug prices.

References

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